

381. (New) A method as in claim 379, comprising allowing the first species to bind to the second species after allowing the first species to be fastened to the first colloid particle.
382. (New) A method as in claim 379, comprising allowing the first species to bind to the second species before allowing the first species to be fastened to the first colloid particle.
383. (New) A method as in claim 276, wherein the allowing step comprises allowing the first and second species to specifically bind to each other.
384. (New) A method as in claim 276, wherein at least one of the first chemical or biological species or second chemical or biological species is fastened to or adapted to be fastened to the first or second colloid particle, respectively, via at least one of a carboxylate group, EDC/NHS chemistry, a nucleic acid sequence, or affinity tag interaction.
385. (New) A method as in claim 276, wherein at least one of the first chemical or biological species or second chemical or biological species is fastened to or adapted to be fastened to the first or second colloid particle, respectively, via affinity tag interaction.
386. (New) A method as in claim 276, wherein at least one of the first chemical or biological species or second chemical or biological species is fastened to or adapted to be fastened to the first or second colloid particle, respectively, via affinity tag interaction comprising a metal binding tag.
387. (New) A method as in claim 276, wherein the binding interaction is a biological binding interaction.
388. (New) A method as in claim 387, wherein the biological binding interaction comprises binding between a protein and a nucleic acid.
389. (New) A method as in claim 276, wherein at least one of the first and second species is a protein.

390. (New) A method as in claim 276, wherein at least one of the first and second species is a synthetic molecule.

391. (New) A method as in claim 387, wherein the binding interaction comprises binding between a molecule and its specific binding partner.

392. (New) A method as in claim 276, wherein the first species and the second species are the same species type.

393. (New) A method as in claim 276, wherein the first species and the second species are the same.

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cont. 394. (New) A method as in claim 276, wherein the first colloid particle and the second colloid particle are the same type of colloid particle.

395. (New) A method as in claim 276, wherein each of the first colloid particle and the second colloid particle is a gold colloid particle.

396. (New) A method as in claim 276, wherein the binding interaction is affected by an enzyme. <sup>broad</sup>

397. (New) A method as in claim 396, wherein the enzyme comprises caspase.

398. (New) A method as in claim 396, wherein the enzyme comprises calpain.

399. (New) A method as in claim 396, comprising carrying out the method in the presence of a drug candidate for affecting enzyme activity.

*No method steps*

400. (New) A method as in claim 276, wherein the first colloid particle carries an immobilized emissive or absorptive species.

401. (New) A method as in claim 400, wherein the second colloid particle carries an affecting species having the ability to affect emission or absorption of the immobilized emissive or absorptive species.

402. (New) A method as in claim 401, wherein the determining step comprises determining the affecting species' ability to affect the emission or absorption of the immobilized emissive or absorptive species.

403. (New) A method as in claim 276, wherein the binding interaction comprises binding of the first and second species to a common entity, the allowing step comprising allowing the first and second species to bind to the common entity.

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ent. 404. (New) A method as in claim 403, wherein the common entity comprises a colloid particle.

405. (New) A method as in claim 403, wherein the common entity comprises biological material.

406. (New) A method as in claim 405, wherein the biological material comprises patient biological material.

407. (New) A method as in claim 405, wherein the biological material comprises a tumor.

408. (New) A method as in claim 405, wherein the biological material comprises a cell.

409. (New) A method as in claim 405, wherein the biological material comprises a protein complex.

410. (New) A method as in claim 403, wherein the common entity comprises an aggregate-forming species.

411. (New) A method as in claim 403, wherein the common entity comprises a precursor of an aggregate-forming species.

412. (New) A method as in claim 403, wherein the common entity comprises a candidate drug.

413. (New) A method as in claim 276, comprising allowing the binding interaction to take place in the presence of a candidate drug.

414. (New) A method as in claim 413, the determining step comprising determining the effect of the candidate drug on the binding interaction.

415. (New) A method as in claim 413, wherein the candidate drug comprises a candidate drug for inhibiting neurodegenerative disease.

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cont. 416. (New) A method as in claim 276, wherein the first species comprises an A $\beta$  peptide.

417. (New) A method as in claim 403, wherein the common entity comprises an A $\beta$  peptide.

418. (New) A method as in claim 417, wherein the first species comprises an A $\beta$  peptide.

419. (New) A method as in claim 276, wherein the first species comprises an RGD motif.

420. (New) A method as in claim 276, wherein each of the first and second species comprises an antibody, each recognizing a different epitope on a common chemical or biological entity.

421. (New) A method as in claim 403, wherein the common entity comprises patient material.

422. (New) A method as in claim 276, wherein the first species comprises vitronectin.

423. (New) A method as in claim 403, wherein the common entity comprises endostatin.

424. (New) A method as in claim 276, further comprising exposing a sample suspected of containing an analyte to the first and second chemical or biological species, wherein the analyte is suspected of affecting the binding interaction.

425. (New) A method as in claim 424, wherein the analyte enhances the binding interaction.

426. (New) A method as in claim 424, wherein the analyte disrupts the binding interaction.

427. (New) A method as in claim 424, wherein the analyte binds to the first species, thereby affecting the binding interaction.

428. (New) A method as in claim 424, wherein the analyte binds to a common entity to which each of the first and second species is able to bind.

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cont. 429. (New) A method as in claim 424, wherein the analyte binds to a common entity, thereby disrupting binding ability between the analyte at least one of the first or second species.

430. (New) A method as in claim 424, wherein the analyte comprises a candidate drug.

431. (New) A method as in claim 430, wherein the candidate drug comprises a candidate drug for inhibiting neurodegenerative disease.

432. (New) A method as in claim 424, wherein the analyte comprises an antibody.

433. (New) A method as in claim 276, wherein the allowing step comprises allowing the first and second species each to specifically bind to a common biological target.

434. (New) A method as in claim 276, wherein the allowing step comprises allowing an enzyme to affect the binding interaction between the first and second species, and the determining step comprises determining the effect of the enzyme on the binding interaction.

435. (New) A method as in claim 403, wherein the common entity is an enzyme substrate, the method comprising exposing the enzyme substrate to an enzyme and an agent suspected of inhibiting the enzyme, the method further comprising determining immobilization of the first colloid particle with respect to the second colloid particle.

436. (New) A method as in claim 276, wherein the first and second species can be linked by an enzyme, the method comprising exposing the first and second species to an enzyme and a suspected inhibitor of the enzyme.

437. (New) A method as in claim 276, further comprising exposing a sample suspected of containing an analyte to the first and second chemical or biological species, wherein the first and second chemical or biological species each have the ability to fasten to the analyte.

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cont. 438. (New) A method as in claim 437, wherein the determining step comprises determining immobilization of the first colloid particle with respect to the second colloid particle indicative of the presence of the analyte in the sample.

439. (New) A method as in claim 437, wherein the first and second chemical or biological species do not have the ability to directly bind to each other.

440. (New) A method as in claim 437, wherein the analyte comprises a candidate drug.

441. (New) A method as in claim 437, wherein the sample comprises a protein, peptide, nucleic acid, or enzyme, and is naturally-occurring, synthetic, or cloned.

442. (New) A method as in claim 276, further comprising exposing, to the first and second chemical or biological species, a sample that contains or is suspected of containing an aggregate-forming species; or contains or is suspected of containing a precursor of an aggregate-forming species; or is able to produce or suspected of being able to produce aggregate-forming species; or is able to produce or suspected of being able to produced a precursor of an aggregate-forming species.

443. (New) A method as in claim 442, wherein the sample contains or is suspected of containing a disease associated aggregate-forming species.

444. (New) A method as in claim 443, wherein the disease is neurodegenerative disease.

445. (New) A method as in claim 442, wherein the sample comprises a protein or peptide that is an aggregate-forming species.

446. (New) A method as in claim 442, wherein the sample comprises a precursor of a protein or peptide that is an aggregate-forming species.

447. (New) A method as in claim 442, wherein the sample comprises a species derived from a cell that produces a protein or peptide that is an aggregate-forming species.

448. (New) A method as in claim 447, wherein the sample comprises material secreted from the cell.

449. (New) A method as in claim 447, wherein the sample comprises a lysate of the cell or a fraction thereof.

450. (New) A method as in claim 276, further comprising:

determining a first observable feature of the particles indicative of a first degree of immobilization of the first colloid particle with respect to the second colloid particle at a first point in time; and

determining a second observable feature of the particles indicative of a second degree of immobilization of the first colloid particle with respect to the second colloid particle at a second point in time.

451. (New) A method as in claim 450, wherein the first and second points in time differ by at least one day.

452. (New) A method as in claim 450, wherein the first and second points in time differ by at least 1.5 days.

453. (New) A method as in claim 450, wherein the first and second points in time differ by at least two days.

454. (New) A method as in claim 450, wherein the first and second points in time differ by no more than 20 minutes.

455. (New) A method as in claim 450, wherein the first and second points in time differ by no more than 10 minutes.

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cont. 456. (New) A method as in claim 450, wherein the first and second points in time differ by no more than 5 minutes.

457. (New) A method as in claim 450, wherein the first and second points in time differ by no more than one minute.

458. (New) A method as in claim 450, wherein the first and second points in time differ by no more than 30 seconds.

459. (New) A method as in claim 276, wherein the determining step comprises determining an observable feature indicative of the immobilization of the first colloid particle with respect to the second colloid particle.

460. (New) A method as in claim 459, wherein the observable feature comprises a change visible to the human eye.

461. (New) A method as in claim 460, wherein the visible change comprises the aggregation of particles.



462. (New) A method as in claim 460, wherein the visible change comprises a color change.

463. (New) A method as in claim 276, wherein the determining step comprises determining an extent of immobilization of the first colloid particle with respect to the second colloid particle indicative of the presence of an aggregate-forming species.

464. (New) A method as in claim 463, wherein the determining step comprises digitizing an image of the sample, then using pattern recognition to determine the presence of aggregates.

465. (New) A method as in claim 464, wherein the presence of aggregates is correlated with a disease.

466. (New) A method as in claim 465, wherein the disease is neurodegenerative disease.

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cont. 467. (New) A method as in claim 276, wherein the first colloid particle comprises a signaling entity.

468. (New) A method as in claim 276, wherein the first colloid particle itself is a signaling entity.

469. (New) A method as in claim 276, wherein the first colloid particle comprises an emissive or absorptive property.

470. (New) A method as in claim 276, wherein the first colloid particle comprises a plurality of auxiliary signaling entities.

471. (New) A method as in claim 470, wherein the plurality of auxiliary signaling entities are covalently fastened to the first colloid particle.

472. (New) A method as in claim 467, wherein the signaling entity is an electroactive species.

473. (New) A method as in claim 467, wherein the signaling entity is a metallocene.

474. (New) A method as in claim 467, wherein the signaling entity is a ferrocene or a ferrocene derivative.

475. (New) A method as in claim 467, wherein the signaling entity comprises an entity selected from the group consisting of a dye, a pigment, an electroactive molecule, a fluorescent moiety, an up-regulating phosphor, an enzyme-fastened signaling moiety, horseradish peroxidase, alkaline phosphatase, an electrochemiluminescent entity, and a semiconductor.

476. (New) A method as in claim 467, wherein the signaling entity is a multiple signaling entity.

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ent 477. (New) A method as in claim 276, wherein each of the first and second colloid particles comprises a signaling entity.

478. (New) A method as in claim 276, wherein the first colloid particle carries a first immobilized signaling entity and the second colloid particle carries a second signaling entity, the first signaling entity having the ability to enhance a signaling property of the second signaling entity.

479. (New) A method as in claim 276, wherein the first colloid particle carries a first immobilized signaling entity and the second colloid particle carries a second signaling entity, the first signaling entity having the ability to inhibit a signaling property of the second signaling entity.

480. (New) A method as in claim 276, wherein each of the first and second colloid particles itself is a signaling entity.

481. (New) A method as in claim 276, wherein each of the first and second colloid particles